	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
9	BRS	L10	289	bactericidal$1permeability adj increasing adj protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:11			0
10	BRS	L11	32	limulus adj anti-LPS adj factor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:12			0
11	BRS	L12	3	3 same (10 or 11) same (hybrid adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:14			0
12	BRS	L13	56	(variant or mutant) same 3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:14			0
13	BRS	L14	6	13 same (1 or 2)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:15			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2148	septicemia	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 12:57			0
2	BRS	L2	10939	sepsis or (septic adj shock)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 12:58			0
3	BRS	L3	2496	lbp or (liposaccharide adj binding adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 12:58			0
4	BRS	L5	53	3 same (1 or 2)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:08			0
5	BRS	L6	13260	(gram-positive adj bacteria) or (gram-negative adj bacteria)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:09			0
6	BRS	L7	150827	trauma or injury	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:09			0
7	BRS	L8	4692	(1 or 2) same (6 or 7)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:10			0
8	BRS	L9	25	8 same 3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/20 13:10			0

> d his

(FILE 'HOME' ENTERED AT 16:07:06 ON 20 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
16:07:35 ON 20 NOV 2002
L1 55452 S SEPTICEMIA
L2 151026 S SEPSIS OR (SEPTIC SHOCK)
L3 4847 S (LIPOSACCHARIDE BINDING PROTEIN) OR LBP
L4 349 S (L1 OR L2) (P) L3
L5 91545 S (GRAM-POSITIVE BACTERIA) OR (GRAM-NEGATIVE BACTERIA)
L6 1413783 S TRAUMA OR INJURY
L7 106 S L4 (P) (L5 OR L6)
L8 38 DUPLICATE REMOVE L7 (68 DUPLICATES REMOVED)
L9 16 S L8 AND PY<1998
L10 2090 S BACTERICIDAL (W) PERMEABILITY (W) INCREASING (W) PROTEIN
L11 48 S LIMULUS ANTI-LPS FACTOR
L12 267 S L3 (P) (L10 OR L11)
L13 4 S L12 (P) (HYBRID PROTEIN)
L14 2 DUPLICATE REMOVE L13 (2 DUPLICATES REMOVED)

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COST IN U.S. DOLLARS

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FILE 'HOME' ENTERED AT 16:07:06 ON 20 NOV 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'CAPLUS' ENTERED AT 16:07:35 ON 20 NOV 2002
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FILE 'AGRICOLA' ENTERED AT 16:07:35 ON 20 NOV 2002

=> s septicemia
L1       55452 SEPTICEMIA

=> s sepsis or (septic shock)
L2      151026 SEPSIS OR (SEPTIC SHOCK)

=> s (liposaccharide binding protein) or lbp
L3        4847 (LIPOSACCHARIDE BINDING PROTEIN) OR LBP

=> s (l1 or l2) (p) l3
L4         349 (L1 OR L2) (P) L3

=> s (gram-positive bacteria) or (gram-negative bacteria)
L5       91545 (GRAM-POSITIVE BACTERIA) OR (GRAM-NEGATIVE BACTERIA)

=> s trauma or injury
L6     1413783 TRAUMA OR INJURY

=> s l4 (p) (l5 or l6)
L7         106 L4 (P) (L5 OR L6)

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8           38 DUPLICATE REMOVE L7 (68 DUPLICATES REMOVED)

=> s l8 and py<1998
   3 FILES SEARCHED...
   5 FILES SEARCHED...
L9           16 L8 AND PY<1998

=> d l9 1-16 ibib abs

L9   ANSWER 1 OF 16     MEDLINE
ACCESSION NUMBER:    97064226     MEDLINE
DOCUMENT NUMBER:     97064226   PubMed ID: 8906845
TITLE:               Effects of site-directed mutagenesis of basic residues (Arg
                     94, Lys 95, Lys 99) of lipopolysaccharide (LPS)-binding
                     protein on binding and transfer of LPS and subsequent
                     immune cell activation.
AUTHOR:              Lamping N; Hoess A; Yu B; Park T C; Kirschning C J; Pfeil
                     D; Reuter D; Wright S D; Herrmann F; Schumann R R
CORPORATE SOURCE:    Molecular Sepsis Research Laboratory, Max-Delbruck-Center
                     for Molecular Medicine, Berlin, Germany.
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CONTRACT NUMBER: AI30556 (NIAID)
K08AI (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, ***(1996 Nov 15)*** 157 (10) 4648-56.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961231

AB LPS-binding protein (***LBP***) is a 60-kDa acute phase glycoprotein capable of binding the LPS of ***Gram*** - ***negative*** ***bacteria*** and facilitating its diffusion. This process is thought to be of potential importance in inflammatory reactions and pathogenic states such as ***septic*** ***shock*** syndrome. Here, we report on the identification of a LPS binding domain within the ***LBP*** molecule and on the identification of single amino acids important for binding of LPS by ***LBP*** . Several synthetic ***LBP*** peptides inhibited LPS- ***LBP*** interaction, and amino acids Arg 94 and Lys 95 were centrally located in these inhibitory peptides. ***LBP*** mutants with amino acid exchanges within this region were expressed and tested in five different functional assays: binding to immobilized LPS; facilitation of binding of LPS aggregates to monocytes; transfer of LPS monomers from aggregates to soluble CD14; transfer of soluble CD14-bound LPS monomers to high density lipoprotein (HDL); and enhancement of LPS-induced cell activation. The double mutant Glu 94/Glu 95 was completely lacking LPS binding, transfer, and cell stimulatory activity, indicating that the integrity of amino acids 94 and 95 is required for ***LBP*** function. While mutations of amino acids Arg 94 or Lys 95 into alanine reduced the LPS binding activity of ***LBP*** dramatically, the ability to facilitate binding of LPS aggregates to membrane CD14 at the cell surface was retained. These findings emphasize the distinction between binding of LPS aggregates to cells, which is not associated with cell stimulation, and binding of LPS monomers to CD14, which leads to cell stimulation.

L9 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 96430818 MEDLINE
DOCUMENT NUMBER: 96430818 PubMed ID: 8833900
TITLE: Antibodies against CD14 protect primates from endotoxin-induced shock.
AUTHOR: Leturcq D J; Moriarty A M; Talbott G; Winn R K; Martin T R; Ulevitch R J
CORPORATE SOURCE: R.W. Johnson Pharmaceutical Research Institute, San Diego, California 92121, USA.
CONTRACT NUMBER: AI151136 (NIAID)
GM28485 (NIGMS)
GM37696 (NIGMS)
+
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, ***(1996 Oct 1)*** 98 (7) 1533-8.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961119

AB Lipopolysaccharide (LPS), residing in the outer membrane of all ***gram*** - ***negative*** ***bacteria*** , is considered a major initiating factor of the gram-negative ***septic*** ***shock*** syndrome in humans. LPS forms a complex with the LPS binding protein (***LBP***) in plasma, and LPS- ***LBP*** complexes engage a specific receptor, CD14, on the surface of myeloid cells, leading to the production of potent proinflammatory cytokines. The major goal of this study was to test the importance of the CD14 pathway in vivo in a primate model that is similar to human ***septic*** ***shock*** . Primates were pretreated with one of two different inhibitory anti-CD14 mAbs, then

challenged with intravenous endotoxin (375 microg/kg/h) for 8 h. The anti-CD14 treatment regimens were successful in preventing [redacted] found hypotension, reducing plasma cytokine levels (TNF-alpha, IL-1beta, IL-6, and IL-8), and inhibiting the alteration in lung epithelial permeability that occurred in animals treated with LPS and an isotype-matched control antibody. These results demonstrate for the first time the importance of the CD14 pathway in a primate model that is similar to human ***septic*** ***shock*** . Inhibition of the CD14 pathway represents a novel therapeutic approach to treating this life-threatening condition.

L9 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 95365948 MEDLINE
DOCUMENT NUMBER: 95365948 PubMed ID: 7638748
TITLE: Peptide derivatives of three distinct lipopolysaccharide binding proteins inhibit lipopolysaccharide-induced tumor necrosis factor-alpha secretion in vitro.
AUTHOR: Battafaraono R J; Dahlberg P S; Ratz C A; Johnston J W; Gray B H; Haseman J R; Mayo K H; Dunn D L
CORPORATE SOURCE: Department of Surgery, University of Minnesota, Minneapolis, USA.
CONTRACT NUMBER: R01 GM32414 (NIGMS)
SOURCE: SURGERY, ***(1995 Aug)*** 118 (2) 318-24.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19950921
Entered Medline: 19950913

AB BACKGROUND. Bactericidal permeability increasing protein (BPI), Limulus anti-lipopolysaccharide factor (LALF), and lipopolysaccharide binding protein (***LBP***) are three distinct proteins that bind to lipopolysaccharide (LPS). Intriguingly, binding of BPI and LALF to LPS results in neutralization of LPS activity, whereas the binding of ***LBP*** to LPS creates a complex that results in augmentation of LPS activity. Despite their different effector functions, we hypothesized that peptides based on the sequences of the proposed LPS-binding motif from each protein would neutralize LPS in vitro. METHODS. Three peptide sequences, each 27 amino acids in length, of the proposed LPS-binding motif of BPI (BG38), LALF (BG42), and ***LBP*** (BG43) were synthesized. These peptides were then tested for their: (1) ability to inhibit macrophage secretion of TNF-alpha after stimulation by LPS derived from Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Serratia marcescens; and (2) bactericidal activity against these same four ***gram*** - ***negative*** ***bacteria*** in vitro. RESULTS. Synthetic peptides BG38 (BPI-derived), BG42 (LALF-derived), and BG43 (***LBP*** -derived) but not control peptide significantly inhibited LPS-induced tumor necrosis factor-alpha secretion by macrophages and mediated the lysis of ***gram*** - ***negative*** ***bacteria*** in vitro. In addition, preincubation of LPS with peptide BG38 mediated complete protection subsequent to lethal endotoxin challenge. CONCLUSIONS. These data demonstrate that small peptides derived from BPI, LALF, and ***LBP*** retained significant endotoxin-neutralizing and bactericidal activity against many different ***gram*** - ***negative*** ***bacteria*** in vitro. Identification of this conserved LPS-binding region within each protein may aid in the development of new immunomodulatory reagents for use as adjuvant therapy in the treatment of gram-negative bacterial ***sepsis*** .

L9 ANSWER 4 OF 16 MEDLINE
ACCESSION NUMBER: 95336686 MEDLINE
DOCUMENT NUMBER: 95336686 PubMed ID: 7542010
TITLE: Receptor-dependent mechanisms of cell stimulation by bacterial endotoxin.
AUTHOR: Ulevitch R J; Tobias P S
CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, California 92037, USA.
CONTRACT NUMBER: AI15136 (NIAID)
GM28485 (NIGMS)
GM3769 (NIGMS)

SOURCE: ANNUAL REVIEW OF IMMUNOLOGY, ***(1995)*** 3 437-57.
Ref: 102
Journal code: 8309206. ISSN: 0732-0582.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950905
Last Updated on STN: 19980206
Entered Medline: 19950818

AB In humans and experimental animals the presence of bacterial lipopolysaccharide (endotoxin, LPS) signals the presence of ***gram*** - ***negative*** ***bacteria*** . Recognition of LPS triggers gene induction by myeloid and nonmyeloid lineage cells. These inducible genes encode proteins that include cytokines, adhesive proteins, and enzymes that produce low molecular weight proinflammatory mediators. Together the products of these inducible genes upregulate host defense systems that participate in eliminating the bacterial infection. Unfortunately, these same mediators contribute to a serious human disease known as ***septic*** ***shock*** . Considerable progress has been made during the past decade in determining the sources, identities, and sequence of release of these mediators. In contrast, until recently, marked gaps in our knowledge existed regarding the identity of the LPS receptor and intracellular signaling pathways responsible for LPS-induced cell activation. The discovery in 1986 of a plasma protein termed LPS binding protein (***LBP***) led to the discovery of unanticipated mechanisms of LPS-induced cell activation. CD14 was found as a soluble serum protein or as a glycosylphosphatidylinositol (GPI)-anchored protein of myeloid lineage cells; it now occupies a key role in LPS-induced cell activation as we understand it today. Here we discuss how ***LBP*** enables LPS binding to CD14 and how complexes of LPS and soluble or GPI-anchored CD14 participate in cell activation. We also review the evidence supporting a model for a functional LPS receptor of myeloid cells, which is multimeric, comprised of GPI-anchored CD14 and a presently unidentified transmembrane protein that together bind LPS and initiate cell activation via kinase cascades.

L9 ANSWER 5 OF 16 MEDLINE
ACCESSION NUMBER: 95057113 MEDLINE
DOCUMENT NUMBER: 95057113 PubMed ID: 7526045
TITLE: Transforming growth factor-beta 1 lowers the CD14 content of monocytes.
AUTHOR: Hamon G; Mulloy R H; Chen G; Chow R; Birkenmaier C; Horn J K
CORPORATE SOURCE: Department of Surgery, San Francisco General Hospital, University of California 94143.
CONTRACT NUMBER: R49/CCR604382
SOURCE: JOURNAL OF SURGICAL RESEARCH, ***(1994 Nov)*** 57 (5) 574-8.
Journal code: 0376340. ISSN: 0022-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19960129
Entered Medline: 19941208

AB Marked elevation of transforming growth factor-beta 1 (TGF-beta 1) has been demonstrated clinically following ***injury*** and in ***sepsis*** . While alterations in the monocyte binding site (CD14) for the lipopolysaccharide (LPS)-lipopolysaccharide binding protein (***LBP***) complex have been noted with exposure to LPS, immune complexes, gamma-interferon, and IL-4, it is not known whether TGF-beta 1 can alter CD14 expression. To study the effect of TGF-beta 1 on monocyte CD14 expression, human leukocytes were isolated from healthy donors with discontinuous gradient centrifugation and incubated at 37 degrees C for 2 and 24 hr with increasing doses of purified human platelet TGF-beta 1.

Monocytes were immunofluorescently stained with monoclonal antibodies recognizing CD14 and CD16. [redacted]e cells were analyzed by flow [redacted]ometry. At 2 hr, 50 ng/ml TGF-beta 1 significantly lowered CD14 expression (51%, P = 0.043). At 24 hr, there was no significant difference between cells stimulated by TGF-beta 1 and control cells. To confirm that TGF-beta 1 was active at 24 hr, we examined levels of CD16. CD16 expression was increased by 10 ng/ml of TGF-beta 1. These observations suggest that high physiologic concentrations of TGF-beta 1 cause early monocyte suppression of CD14. Thus, CD14 may be marker for the transition of monocytes to macrophages and TGF-beta 1 may be responsible for the down-regulation of CD14 expression observed in monocytes obtained from septic patients.

L9 ANSWER 6 OF 16 MEDLINE
ACCESSION NUMBER: 94178922 MEDLINE
DOCUMENT NUMBER: 94178922 PubMed ID: 8132325
TITLE: Competition between rBPI23, a recombinant fragment of bactericidal/permeability-increasing protein, and lipopolysaccharide (LPS)-binding protein for binding to LPS and gram-negative bacteria.
AUTHOR: Gazzano-Santoro H; Meszaros K; Birr C; Carroll S F; Theofan G; Horwitz A H; Lim E; Aberle S; Kasler H; Parent J B
CORPORATE SOURCE: Department of Sepsis Research, XOMA Corporation, Berkeley, California 94710.
SOURCE: INFECTION AND IMMUNITY, ***(1994 Apr)*** 62 (4) 1185-91.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19940428
Entered Medline: 19940421

AB Lipopolysaccharide (LPS)-binding protein (***LBP***) and bactericidal/permeability-increasing protein (BPI) are two structurally related lipid A-binding proteins with divergent functional activities. ***LBP*** mediates activation of macrophage and other proinflammatory cells. In contrast, BPI has potent bactericidal and LPS-neutralizing activities. A recombinant fragment of BPI (rBPI23) retains the potent biological activities of the holo protein and may represent a novel therapeutic agent for the treatment of gram-negative infections, ***sepsis*** , and endotoxemia. For therapeutic effectiveness in many clinical situations, rBPI23 will have to successfully compete with high serum levels of ***LBP*** for binding to endotoxin and ***gram*** - ***negative*** ***bacteria*** . The relative binding affinities of rBPI23 and human recombinant ***LBP*** (rLBP) for lipid A and ***gram*** - ***negative*** ***bacteria*** were evaluated. The binding of both proteins to lipid A was specific and saturable with apparent Kds of 2.6 nM for rBPI23 and 58 nM for rLBP. rBPI23 was approximately 75-fold more potent than rLBP in inhibiting the binding of 125I-rLBP to lipid A. The binding affinity of rBPI23 (Kd = 70 nM) for Escherichia coli J5 bacteria was also significantly higher than that of rLBP (Kd = 1,050 nM). In addition, rBPI23 at 0.2 micrograms/ml was able to inhibit LPS-induced tumor necrosis factor release from monocytes in the presence of 20 micrograms of rLBP per ml. These results demonstrate that rBPI23 binds more avidly to endotoxin than does rLBP and that, even in the presence of a 100-fold weight excess of rLBP, rBPI23 effectively blocks the proinflammatory response of peripheral blood mononuclear cells to endotoxin.

L9 ANSWER 7 OF 16 MEDLINE
ACCESSION NUMBER: 94052197 MEDLINE
DOCUMENT NUMBER: 94052197 PubMed ID: 7694295
TITLE: Cell-free pool of CD14 mediates activation of transcription factor NF-kappa B by lipopolysaccharide in human endothelial cells.
AUTHOR: Read M A; Cordle S R; Veach R A; Carlisle C D; Hawiger J
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN 37232.
CONTRACT NUMBER: HL-30647 (NHLBI)
HL-30648 (NHLBI)

T32-07186
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, ***(1993 Nov 1)*** 90 (21) 9887-91.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19960129
Entered Medline: 19931209

AB Lipopolysaccharide (LPS), a major envelope component of ***Gram*** -***negative*** ***bacteria*** , is the most frequent causative agent of ***septic*** ***shock*** and disseminated intravascular coagulation. LPS activates both CD14-positive (monocytes, macrophages, polymorphonuclear leukocytes) and CD14-negative (B-cell lines, endothelial cells) cells. CD14, a 55-kDa glycosyl-phosphatidylinositol-anchored membrane protein present on mature myeloid cells, serves as a receptor for LPS in complex with a soluble (serum-derived) LPS-binding protein (***LBP***). In this report, we show that human umbilical vein endothelial cells (HUVEC), which do not express measurable CD14 protein, become 3000-fold more sensitive to LPS-induced activation in the presence of serum, as measured by activation of the transcription factor NF-kappa B and expression of mRNA encoding tissue factor, a procoagulant molecule. This enhanced responsiveness of HUVEC is specifically mediated by the cell-free pool of CD14 (soluble CD14, sCD14) found in serum. The role of sCD14 in HUVEC activation by LPS was established by (i) the blocking effect of monoclonal anti-CD14 antibodies which discriminate between cell-bound and sCD14, (ii) the lack of the serum-enhancing effect after immunodepletion of sCD14, and (iii) establishing a reconstituted system in which recombinant sCD14 was sufficient to enhance the effects of LPS in the absence of serum and without a requirement for ***LBP*** . Thus, this mechanism of endothelial cell activation by LPS involves a cell-free pool of sCD14 most likely shed from CD14-positive cells of the monocytic lineage.

L9 ANSWER 8 OF 16 MEDLINE
ACCESSION NUMBER: 93328265 MEDLINE
DOCUMENT NUMBER: 93328265 PubMed ID: 7687581
TITLE: Endotoxin-mediated endothelial cell injury and activation: role of soluble CD14.
AUTHOR: Arditi M; Zhou J; Dorio R; Rong G W; Goyert S M; Kim K S
CORPORATE SOURCE: Division of Infectious Diseases, Childrens Hospital of Los Angeles 90027.
CONTRACT NUMBER: R01-AI23859 (NIAID)
R01-NS-26310 (NINDS)
SOURCE: INFECTION AND IMMUNITY, ***(1993 Aug)*** 61 (8) 3149-56.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930903
Last Updated on STN: 19980206
Entered Medline: 19930826

AB Vascular endothelial cell (EC) ***injury*** by lipopolysaccharides (LPS) plays a major role in the pathogenesis of gram-negative bacterial ***sepsis*** and endotoxic shock. The studies described here were performed to define further the molecular mechanisms involved in the EC responses to LPS. We showed that serum was required for LPS-mediated cytotoxicity for bovine brain microvessel, pulmonary, and aortic ECs and that anti-human CD14 antibodies completely blocked LPS-mediated cytotoxicity for ECs in the presence of human serum. The addition of a recombinant soluble form of human CD14 to serum-free medium restored the LPS-mediated cytotoxicity, whereas the addition of LPS binding protein (***LBP***), a serum protein that potentiates LPS-induced responses to monocytes, had no effect. A similar dependency on serum or recombinant soluble CD14 (under serum-free conditions) was observed for LPS-induced

secretion of interleukin-6 by human umbilical vein ECs. These findings indicate that soluble CD14 is required for LPS-mediated EC responses independently of LPB, suggesting that serum soluble CD14 represents a naturally occurring agonist for EC responses to LPS.

L9 ANSWER 9 OF 16 MEDLINE
ACCESSION NUMBER: 93308948 MEDLINE
DOCUMENT NUMBER: 93308948 PubMed ID: 1284855
TITLE: Lipopolysaccharide binding protein enhances intratracheally administrated lipopolysaccharide-induced acute lung inflammation via a CD14 receptor.
AUTHOR: Ishii Y; Kitamura S
CORPORATE SOURCE: Department of Pulmonary Medicine, Jichi Medical School, Tochigi, Japan.
SOURCE: NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES, ***(1992 Dec)*** 30 Suppl 225-31. Journal code: 7505737. ISSN: 0301-1542.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930813
Last Updated on STN: 19990129
Entered Medline: 19930730

AB We examined the role of lipopolysaccharide binding protein (***LBP***) in the airspace and the CD14 receptor on alveolar macrophages in TNF alpha production and neutrophil (PMN) sequestration in lungs induced by intratracheal injection of lipopolysaccharide (LPS). LPS alone (Salmonella minnesota wild-type; 20 ng) or LPS + ***LBP*** complex [LPS (20 ng) + rabbit ***LBP*** (500 ng); preincubated for 30 min at 37 degrees C] was injected intratracheally into isolated rabbit lungs perfused with lactate-Ringer-albumin solution. Human PMN (5 x 10(7)) were added to the perfusate after 2 hr perfusion. Samples of lung perfusate were collected every 30 min for 180 min, after which bronchoalveolar lavage (BAL) was also performed. TNF alpha concentration in the perfusate and BAL fluid were determined using a bioassay with L-929 fibroblasts. PMN accumulation in the lung was determined by myeloperoxidase assay of the lung homogenate. LPS alone did not significantly increase TNF alpha production or PMN accumulation in lungs, whereas LPS/ ***LBP*** complex increased TNF alpha concentration in the perfusate and PMN accumulation. Intratracheal injection of anti-CD14 antibody (40 micrograms) with LPS/ ***LBP*** complex prevented TNF alpha production and subsequent PMN sequestration. We conclude that ***LBP*** in the airspace enhances the effect of LPS on TNF alpha production via a CD14-dependent pathway, and this subsequently contributes to PMN sequestration in the lungs. Airspace accumulation of ***LBP*** secondary to increased vascular and epithelial permeability may play a critical role in the development of ***septic*** ***shock*** and lung ***injury*** by promoting TNF alpha production via a CD14-dependent mechanism.

L9 ANSWER 10 OF 16 MEDLINE
ACCESSION NUMBER: 91073473 MEDLINE
DOCUMENT NUMBER: 91073473 PubMed ID: 2254981
TITLE: A new model of macrophage stimulation by bacterial lipopolysaccharide.
AUTHOR: Ulevitch R J; Mathison J C; Schumann R R; Tobias P S
CORPORATE SOURCE: Department of Immunology, Research Institute of Scripps Clinic, La Jolla, CA 92037.
CONTRACT NUMBER: AI15136 (NIAID)
GM28485 (NIGMS)
GM37696 (NIGMS)
+
SOURCE: JOURNAL OF TRAUMA, ***(1990 Dec)*** 30 (12 Suppl) S189-92. Ref: 25
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199101
ENTRY DATE: Entered STN [redacted]9910308
Last Updated on STN: 19910308
Entered Medline: 19910123

AB Infection occurring in patients suffering from severe ***trauma*** or burns often leads to hypotension, disseminated intravascular coagulation, multiorgan failure, and death. These latter pathophysiologic changes often are associated with Gram-negative ***sepsis*** and endotoxemia. Substantial progress has been made in understanding the effector mechanisms for endotoxin (LPS) action with the recognition of the importance of LPS-inducible products of cells of monocytic lineage in mediating LPS-induced ***injury*** . Here we will review recent evidence that supports a model for monocyte/macrophage activation by LPS that involves a plasma protein known as lipopolysaccharide binding protein (***LBP***) and the monocyte differentiation antigen, CD14.

L9 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:510551 CAPLUS
DOCUMENT NUMBER: 129:274546
TITLE: Identification of the lipopolysaccharide (LPS) binding site of LPS binding protein (LBP) by site-directed mutagenesis: evidence for a similar LPS recognition mechanism in different LPS binding proteins
AUTHOR(S): Lamping, N.; Hoess, A.; Yu, B.; Park, T. C.; Wright, S. D.; Kirschning, C. J.; Pfeil, D.; Herrmann, F.; Schumann, R. R.
CORPORATE SOURCE: Labor fuer Molekulare Sepsisforschung, Max-Delbrueck-Centrum fuer, Humboldt-Universitaet zu Berlin, Berlin, Germany
SOURCE: Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, International Congress, 4th, Munich, Mar. 4-8, 1997 (***1997***) , 15-19. Editor(s): Faist, Eugen. Monduzzi Editore: Bologna, Italy.
CODEN: 66MUAY
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Human LPS (endotoxin) Binding Protein (***LBP***) is capable of binding LPS of ***Gram*** - ***neg*** . ***bacteria*** and transporting it to the LPS receptor CD14, a process of potential importance for inflammatory reactions and the ***septic*** ***shock*** syndrome. Here we report on the identification of a region of human ***LBP*** which is involved in ***LBP*** -LPS interaction employing short synthetic ***LBP*** -peptides covering the entire ***LBP*** amino acid sequence. Peptides according to the region of amino acids 81 to 110 exhibited inhibitory activity on LPS- ***LBP*** interaction. ***LBP*** point mutations within this region of ***LBP*** were investigated by different functional assays. A double mutant Glu 94 / Glu 95 failed to display any LPS binding and cell stimulatory activity. Furthermore, exchange of this region of ***LBP*** by the postulated LPS binding regions of bactericidal/permeability increasing protein and Limulus anti-LPS factor (LALF) was able to retain ***LBP*** activity.

L9 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:537632 CAPLUS
DOCUMENT NUMBER: 125:165698
TITLE: Use of MHC-II-binding and/or MHC-II-mimicking molecules for the prevention and treatment of inflammatory diseases
INVENTOR(S): Lauener, Roger Pascal
PATENT ASSIGNEE(S): Laboratoires Om S.A., Switz.; Deutsche Om Arzneimittel Gmbh
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9620215	A2	19960704	WO 1995-EP5164	19951227 <--
WO 9620215	A3	19960810		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2208233	AA	19960704	CA 1995-2208233	19951227 <--
AU 9643476	A1	19960719	AU 1996-43476	19951227 <--
EP 800534	A2	19971015	EP 1995-942207	19951227 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI

CN 1171117	A	19980121	CN 1995-196985	19951227
HU 77468	A2	19980528	HU 1998-269	19951227
JP 10511652	T2	19981110	JP 1995-520220	19951227
BR 9510554	A	19990629	BR 1995-10554	19951227
AU 9963167	A1	20000330	AU 1999-63167	19991206

PRIORITY APPLN. INFO.: EP 1994-203755 A 19941223
WO 1995-EP5164 W 19951227

AB MHC-II-binding and/or MHC-II-mimicking mols. are provided for use in interfering in (1) the interaction between an activation stimulus for MHC-II bearing cells (e.g. phagocytes) and cell-bound MHC-II mols., (2) the interaction between lipopolysaccharide (LPS), or LPS complexed with other mols. such as CD14 and ***LBP*** (LPS-binding protein), and cell-bound MHC-II mols., or (3) the interaction between products from ***gram*** - ***pos*** . ***bacteria*** , or complexes of products from ***gram*** - ***pos*** . ***bacteria*** with mols. such as CD14, and cell-bound MHC-II mols. The MHC-II-binding mol. may be any anti-MHC-II antibody or fragment thereof, or any mol. derived from such an antibody such as humanized, bispecific, or other engineered mols. The MHC-II-binding mol. may be selected from CD14, CD14 fragments, modified CD14, or peptides having MHC-II-binding properties. The title substances are useful for prevention and treatment of inflammatory diseases, e.g. ***septic*** ***shock*** and systemic inflammatory reaction syndrome. Thus, stimulation of MHC-II-pos. (HLA-DR) THP-1 monocytic cells with LPS caused them to secrete TNF-.alpha. and IL-8, whereas HLA-DR-neg. THP-1 cells did not respond. The response by MHC-II-pos. cells was blocked by MHC-II-specific antibodies or by anti-CD14 antibodies.

L9 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1996:255575 CAPLUS
DOCUMENT NUMBER:	124:311874
TITLE:	Lipopolysaccharide (LPS) of Gram-negative bacteria - chemical structure, biological activity and significance in the pathogenicity. III. Lipopolysaccharide as virulence factor of Gram-negative bacteria
AUTHOR(S):	Rozalski, Antoni
CORPORATE SOURCE:	Instytut Mikrobiologii Immunologii, Uniwersytetu Lodzkiego, Lodz, 90-237, Pol.
SOURCE:	Postepy Mikrobiologii (***1995***), 34(3), 339-64 CODEN: PMKMAV; ISSN: 0079-4252
PUBLISHER:	Polskie Towarzystwo Mikrobiologow
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	Polish

AB A review with 127 refs. LPS (endotoxin) derived from the cell wall of ***Gram*** - ***neg*** . ***bacteria*** is an important agent for manifestation of ***sepsis*** in humans. In vivo LPS is bound by different types of proteins which results in the manifestation of ***sepsis*** in human and animal sera: high d. proteins - HDL, lipopolysaccharide binding protein - ***LBP*** , bactericidal/permeability increasing protein -BPI, lactoferrin, septin. LPS- ***LBP*** complexes are recognized by CD14 receptor host cells. Binding of LPS-LPB complexes results in activation of these cells and prodn. of mediators of different origin: .alpha.TNF, Il-1, Il-6, Il-8, prostaglandins, leukotrienes, thromboxan A2 and PAG, as well as free radicals (O2-3, H2O2, NO). Overprodn. of these mediators can be detrimental for host organisms, as it is in Gram-neg. ***septic*** ***shock*** . In this context the biol. effects of the most important mediators of LPS reactions, hypersensitivity and endotoxin tolerance, as

well as LPS mimicry and its catabolism in vivo are described in detail. The results of studies on new possibilities of neutralization of LPS activity in vivo by use of cross-protective antibodies against LPS and TNF, agonists of Il-1 and PAF receptors and some chem. agents (ibuprofen, pentoxifiline) are also assumed.

L9 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:982430 CAPLUS
DOCUMENT NUMBER: 124:764
TITLE: Recombinant preparation of polypeptides of human lipopolysaccharide binding protein and use of the polypeptides for sepsis treatment
INVENTOR(S): Han, Jiahuai; Ulevitch, Richard J.; Tobias, Peter S.
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9525117	A1	19950921	WO 1995-US3384	19950315 <--
W: AU, CA, FI, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5837810	A	19981117	US 1994-215089	19940315
AU 9521868	A1	19951003	AU 1995-21868	19950315 <--

PRIORITY APPLN. INFO.: US 1994-215089 19940315
WO 1995-US3384 19950315

AB A polypeptide fragment of lipopolysaccharide (LPS)-binding protein (***LBP***) that inhibit the binding of LPS released by ***gram*** - ***neg*** . ***bacteria*** into the CD14 receptor is provided. A method of ameliorating symptoms of ***sepsis*** in a subject by administration of an ***LBP*** polypeptide of the invention, or administration of antibody to ***LBP*** polypeptide, or anti-idiotype antibody is also disclosed.

L9 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:759407 CAPLUS
DOCUMENT NUMBER: 123:225264
TITLE: The molecular mechanisms of macrophage activation and the soluble and cellular LPS receptors LBP and CD14
AUTHOR(S): Schumann, R. R.; Kirschning, C.; Lamping, N.; Knopf, H. P.; Herrmann, F.
CORPORATE SOURCE: Max-Delbruck-Centrum fur Molekulare Medizin (MDC), Berlin, 13122, Germany
SOURCE: Molecular Biology of Haematopoiesis, Proceedings of the Symposium on Molecular Biology of Haematopoiesis -- 8th, Basel, July 9-13, 1993 (***1994***), Meeting Date 1993, 155-62. Editor(s): Abraham, Nader G. Intercept: Andover, UK.
CODEN: 61QJAK
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 25 refs. on endotoxin (lipopolysaccharide) recognition events in the context of its role in the organism when ***Gram*** - ***neg*** . ***bacteria*** have invaded. Some of the steps are shown that might lead to Gram-neg. ***sepsis*** and thus could be targets for therapeutic intervention. Expression of ***LBP*** in a baculovirus system will be a tool in studying lipopolysaccharide-induced cell activation and the function and mechanism of ***LBP*** prodn. is studied by anal. of transcriptional activation.

L9 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:594644 CAPLUS
DOCUMENT NUMBER: 121:194644
TITLE: Molecular mechanisms and therapeutical intervention strategies of the sepsis syndrome: Induction-pattern and function of lipopolysaccharide binding protein
AUTHOR(S): Schumann, Ralf R.; Kirschning, C.; Lamping, N.; Knopf, H. -P.; Aberle, H.; Herrmann, F.

CORPORATE SOURCE: Max-Delbruck-Centrum fur Mol. Med. (MDC), Berlin, 13122, Germany
SOURCE: International Congress Series (***1993***), 1042(BIOLOGY OF VITRONECT), 249-56
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 28 refs. Lipopolysaccharide (LPS) or endotoxin, a part of the outer membrane of ***gram*** - ***neg*** . ***bacteria*** , initiates a cascade of events in the host organism when released into the bloodstream. Moderate activation of immune cells by LPS can be beneficial, in an uncontrolled fashion, however, it often leads to severe malfunctions of the organism. Hypotension, fever, multi-organ-failure, disseminated intravascular coagulation and the full gram-neg. shock syndrome can be induced by the entry of even small amts. of LPS into the bloodstream. The ***sepsis*** syndrome has a high mortality rate and as to now no therapeutical intervention strategy has been established. With the recent discovery of binding proteins and receptors for LPS, insight in the endotoxin recognition and cell activation processes has been gained over the last years. Here the LPS binding protein ***LBP*** is discussed, focussing on its synthesis in the liver and the anal. of the promoter region of the gene. Understanding of the complex mechanism of endotoxin recognition might ultimately lead to therapeutical approaches to stop the chain reaction initiated by LPS, that leads to the shock syndrome.

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     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     16:07:35 ON 20 NOV 2002
L1         55452 S SEPTICEMIA
L2        151026 S SEPSIS OR (SEPTIC SHOCK)
L3          4847 S (LIPOSACCHARIDE BINDING PROTEIN) OR LBP
L4           349 S (L1 OR L2) (P) L3
L5         91545 S (GRAM-POSITIVE BACTERIA) OR (GRAM-NEGATIVE BACTERIA)
L6       1413783 S TRAUMA OR INJURY
L7           106 S L4 (P) (L5 OR L6)
L8            38 DUPLICATE REMOVE L7 (68 DUPLICATES REMOVED)
L9            16 S L8 AND PY<1998

=> s bactericidal/permeability increasing protein
MISSING OPERATOR
MISSING OPERATOR
MISSING OPERATOR
MISSING OPERATOR
MISSING OPERATOR
MISSING OPERATOR

=> s bactericidal (w) permeability (w) increasing (w) protein
L10        2090 BACTERICIDAL (W) PERMEABILITY (W) INCREASING (W) PROTEIN

=> s limulus anti-LPS factor
L11          48 LIMULUS ANTI-LPS FACTOR

=> s l3 (p) (l10 or l11)
L12         267 L3 (P) (L10 OR L11)

=> s L12 (p) (hybrid protein)
L13           4 L12 (P) (HYBRID PROTEIN)

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DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, SCISEARCH'
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L14  ANSWER 1 OF 2      MEDLINE                                DUPLICATE 1
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ACCESSION NUMBER: 1998208282 MEDLINE
DOCUMENT NUMBER: 98208282 Med ID: 9548502
TITLE: Interchangeable endotoxin-binding domains in proteins with opposite lipopolysaccharide-dependent activities.
AUTHOR: Schumann R R; Lamping N; Hoess A
CORPORATE SOURCE: Department of Molecular Sepsis Research, Max-Delbruck-Centrum for Molecular Medicine, University Hospital Charite, Humboldt University, Berlin, Germany.
SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Dec 1) 159 (11) 5599-605. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980420

AB Host defense against microorganisms involves proteins that bind specifically to bacterial endotoxins (LPS), causing different cellular effects. Although LPS-binding protein (***LBP***) can enhance LPS activities, while ***bactericidal*** / ***permeability*** - ***increasing*** ***protein*** (BPI) and ***Limulus*** ***anti*** - ***LPS*** ***factor*** (LALF) neutralize LPS, it has been proposed that their LPS-binding domains possess a similar structure. Here, we provide evidence that the ***LBP*** /LPS-binding domain is, as in the LALF structure, solvent exposed and therefore available for LPS binding. Our investigations into the activity of LPS-binding domains of different LPS-binding proteins, in the context of ***LBP*** , provide the first functional analysis of these domains in a whole protein. We constructed domain exchange ***hybrid*** ***proteins*** by substituting 12 amino acids of the ***LBP*** /LPS-binding domain with those of BPI and LALF and expressed them in Chinese hamster ovary cells. Although discrete point mutations within the LPS-binding domain of ***LBP*** disrupted its specific functions, the ***hybrid*** ***proteins*** were still able to bind LPS and, in addition, retained the wild-type ***LBP*** activity of enhancing LPS priming for FMLP-induced oxygen radical production by neutrophils and transferring LPS aggregates to CD14. Although BPI and LALF display opposite activities to ***LBP*** , and LALF does not share any sequence homology with ***LBP*** , our data provide strong evidence that ***LBP*** , BPI, and LALF possess a solvent-exposed, interchangeable LPS binding motif that is functionally independent of LPS transport or neutralization.

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:492022 CAPLUS
DOCUMENT NUMBER: 122:232671
TITLE: Lipopolysaccharide binding protein derivatives, their manufacture with recombinant cells, and their use in treatment of Gram-neg. bacterial infections
INVENTOR(S): Gazzano-Santoro, Helene; Theofan, Georgia; Trown, Patrick W.
PATENT ASSIGNEE(S): Xoma Corp., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500641	A1	19950105	WO 1994-US6931	19940617
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9471756	A1	19950117	AU 1994-71756	19940617
PRIORITY APPLN. INFO.:			US 1993-79510 A	19930617
			WO 1994-US6931 W	19940617

AB Disclosed are novel biol. active lipopolysaccharide binding protein (

LBP) derivs. including ***LBP*** deriv. ***hybrid*** ***proteins*** which are characterized by the ability to bind to and neutralize LPS and which lack the CD14-mediated immunostimulatory properties of holo- ***LBP*** . CDNA's for human ***LBP*** and for (1-197) ***LBP*** , called LBP25 were cloned. Genes for LBP25, for BPI23 [where BPI refers to human ***bactericidal*** / ***permeability*** - ***increasing*** ***protein*** and BPI23 to (1-199)BPI], and hybrid ***LBP*** -BPI proteins were constructed and expressed in CHO cells. Lipid A binding activity and pharmacokinetics of selected proteins were examd. LBP25, unlike ***LBP*** , did not potentiate release of tumor necrosis factor by peripheral blood mononuclear cells and did not mediate LPS-stimulated tissue factor prodn. LBP25 completely inhibited LPS induction of endothelial cell adhesiveness for neutrophils. Addnl., LBP25 was unable to mediate CD14-dependent enhanced binding of bacteria to monocytes.

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:07:35 ON 20 NOV 2002

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L1         55452 S SEPTICEMIA
L2        151026 S SEPSIS OR (SEPTIC SHOCK)
L3          4847 S (LIPOSACCHARIDE BINDING PROTEIN) OR LBP
L4           349 S (L1 OR L2) (P) L3
L5         91545 S (GRAM-POSITIVE BACTERIA) OR (GRAM-NEGATIVE BACTERIA)
L6       1413783 S TRAUMA OR INJURY
L7           106 S L4 (P) (L5 OR L6)
L8            38 DUPLICATE REMOVE L7 (68 DUPLICATES REMOVED)
L9            16 S L8 AND PY<1998
L10         2090 S BACTERICIDAL (W) PERMEABILITY (W) INCREASING (W) PROTEIN
L11           48 S LIMULUS ANTI-LPS FACTOR
L12          267 S L3 (P) (L10 OR L11)
L13            4 S L12 (P) (HYBRID PROTEIN)
L14            2 DUPLICATE REMOVE L13 (2 DUPLICATES REMOVED)
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	86.15	86.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.34	-4.34

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